

ABSTRACT OF THE DISCLOSURE

The present invention provides a method for identifying a thermostable polymerase having altered fidelity. The method consists of generating a random 5 population of polymerase mutants by mutating at least one amino acid residue of a thermostable polymerase and screening the population for one or more active polymerase mutants by genetic selection. For example, the invention provides a method for identifying a 10 thermostable polymerase having altered fidelity by mutating at least one amino acid residue in an active site  $\beta$ -helix of a thermostable polymerase. The invention also provides thermostable polymerases and nucleic acids encoding thermostable polymerases having altered 15 fidelity, for example, high fidelity polymerases and low fidelity polymerases. The invention additionally provides a method for identifying one or more mutations in a gene by amplifying the gene with a high fidelity polymerase. The invention further provides a method for 20 accurately copying repetitive nucleotide sequences using a high fidelity polymerase mutant. The invention also provides a method for diagnosing a genetic disease using a high fidelity polymerase mutant. The invention further provides a method for randomly mutagenizing a gene by 25 amplifying the gene using a low fidelity polymerase mutant.

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